

Online supplement

Methods

Pulmonary function

For all participants post bronchodilator forced expiratory volume in the first second (FEV1) and forced vital capacity were determined using spirometry (Master Screen PFT Pro, CareFusion, Houten, the Netherlands) according to the guidelines of the European Respiratory Society.¹

Borg symptom scores

Participants were asked to score the degree of dyspnea and fatigue using a modified Borg symptom score ranging from 0 (no symptoms) to 10 points (worst symptoms) at different time points.² Borg scores for part 1 of the study were obtained at three time points: 1) right before the strength test, 2) right before the endurance test, 3) directly after the endurance test (see flow chart figure E2). Borg scores for part 1 of the study were obtained before and after the protocol (see flow chart figure E3)

Strength and endurance testing

Strength and endurance of the quadriceps muscle and biceps muscle were evaluated on a dynamometer (Biodex system 3, Biodex corporation, Shirley, New York, U.S.) using an adaptation of a protocol previously described by Allaire et al.³ A flow chart of strength and endurance testing is provided in figure E2.

Dynamometer set-up

All muscle function experiments started with establishment of the correct seating position. For measurement of the QF the seating position was adjusted to ensure that the lateral epicondyle of the right femur was centred with the axis of rotation of the lever arm. The hip and knee angle were adjusted to 90°. The lower leg was firmly attached to the lever arm with a padded Velcro strap. For measurement of the BB the right shoulder was adjusted to 30° exorotation, with an elbow angle of 90°. The wrist was firmly attached to the lever arm with a padded Velcro strap. To prevent for extraneous movement during the isometric contractions, straps were secured across the waist and shoulders.

Muscle strength testing

In order to determine the maximal voluntary contraction (MVC), subjects performed three maximal contractions, each lasting three seconds and separated by 120 seconds rest. A countdown was given, followed by strong verbal encouragement to maximize torque. In case of an MVC variability of >10% we asked participants to perform a fourth maneuver. All participants were able to produce three reproducible maximal contractions in their first three or four attempts. The highest value of the contractions was considered as the MVC.

Muscle endurance testing

After three minutes of rest following the MVC manoeuvres, subjects were instructed to maintain a isometric force representing 60% of their MVC until exhaustion. A computer screen served as a feedback mechanism to help subjects maintain the determined submaximal tension. Subjects were strongly encouraged to pursue until tension drop to 50% of MVC. Peripheral muscle endurance was thus assessed by the time to fatigue, defined as the time at which the

isometric contraction reached 50% MVC. Mean torque (Nm) and the coefficient of variation (CV) of the torque (%) during the endurance test were similar between COPD patients and healthy subjects for the quadriceps muscle (COPD mean torque: 62.2 ± 2.8 Nm, healthy mean torque: 61.2 ± 1.7 Nm, COPD CV: $6.4 \pm 2.1\%$, healthy CV: $6.2 \pm 2.1\%$) and for the biceps muscle (COPD mean torque: 63.0 ± 3.7 Nm, healthy mean torque: 62.1 ± 3.4 Nm, COPD CV: $2.9 \pm 1.0\%$, healthy CV: $2.7 \pm 0.9\%$). An example of torque output during the endurance test of a random COPD patient is shown in figure E4.

References

- 1 Quanjer PH, Tammeling GJ, Cotes JE, et al. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993; 16:5-40
- 2 Vaes AW, Wouters EF, Franssen FM, et al. Task-related oxygen uptake during domestic activities of daily life in patients with COPD and healthy elderly subjects. *Chest* 2011; 140:970-979
- 3 Allaire J, Maltais F, Doyon JF, et al. Peripheral muscle endurance and the oxidative profile of the quadriceps in patients with COPD. *Thorax* 2004; 59:673-678
- 4 Theou O, Jones GR, Vandervoort AA, et al. Daily muscle activity and quiescence in non-frail, pre-frail, and frail older women. *Exp Gerontol* 2010; 45:909-917

Figure legends

Figure E1: Subject holding the arm still at different arm elevation levels (low: $\leq 45^\circ$ (A), medium: $45-90^\circ$ (B), high: $>90^\circ$ (C)). The CAM was attached to the arm.

Figure E2: Flow chart muscle strength and endurance testing for quadriceps muscle of the lower extremity and the biceps muscle of the upper extremity.

Figure E3: Flow chart protocol for the assessment of daily arm activities in the laboratory setting.

Figure E4: Example of torque output during the endurance test of the biceps muscle (A) and the quadriceps muscle (B). The subject is a COPD patient.

Figure E5: Subject equipped with sensors for the assessment of daily arm activities in the laboratory setting. The cables from the EMG electrodes were taped to the skin and placed into the PASAQ which was worn in a small backpack on the back of the participant. The CAM was attached above the elbow.

Figure E6: Positions in which maximal voluntary effort of the trapezius, biceps and deltoid muscle were performed. The large arrows represent the direction of force. The muscle involved is represented in red.

Figure E7: Mean \pm SD of borg scores for fatigue and dyspnea at the beginning of the endurance test and the change in scores after the endurance test for the quadriceps and biceps muscles. Scores are presented for COPD patients (black bars) and healthy subjects (grey bars). *: $p < 0.05$.

Figure E8: Bars represent percentage of time spent on dynamic activities (black), weight bearing postures (grey) and non-weight bearing postures (striped).

Figure E9: Mean \pm SD of borg scores for fatigue and dyspnea at the beginning of the protocol for assessment of daily arm activities in the laboratory setting the change in scores after the protocol. Scores are presented for COPD patients (black bars) and healthy subjects (grey bars). *: $p < 0.05$.

Figure E10: Log(10) transformed relative muscle effort (%) of the trapezius, biceps and deltoid muscles for the arm category 'low elevation and medium intensity' (typically the arm category during walking). Data is presented for COPD patients and healthy subjects during leg activity (white rounds) and without leg activity (e.g. sitting and standing) (black rounds).

Figure E1

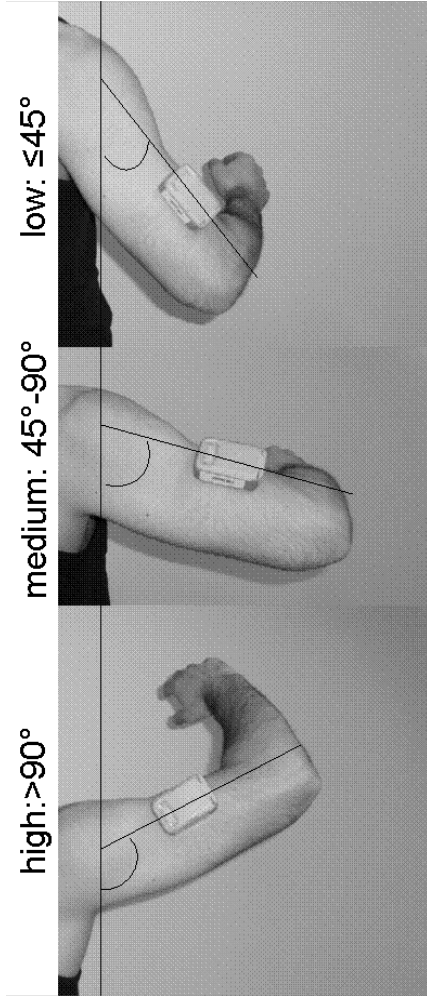
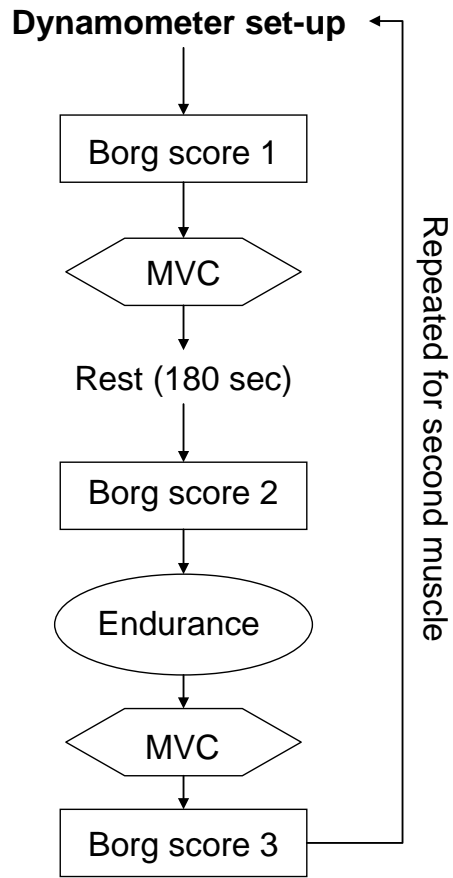


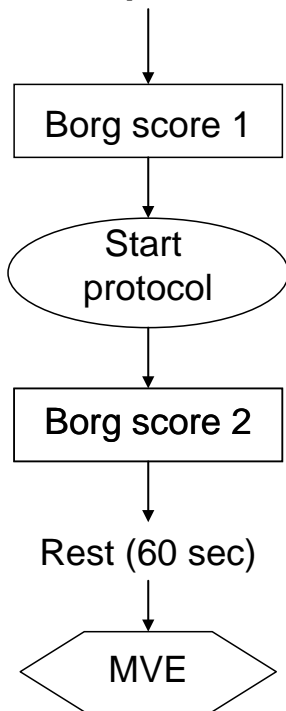
Figure E2:



Abbreviation: MVC: maximal voluntary contraction

Figure E3:

Sensor placement



Abbrivation: MVE: maximal muscle effort.

Figure E4:

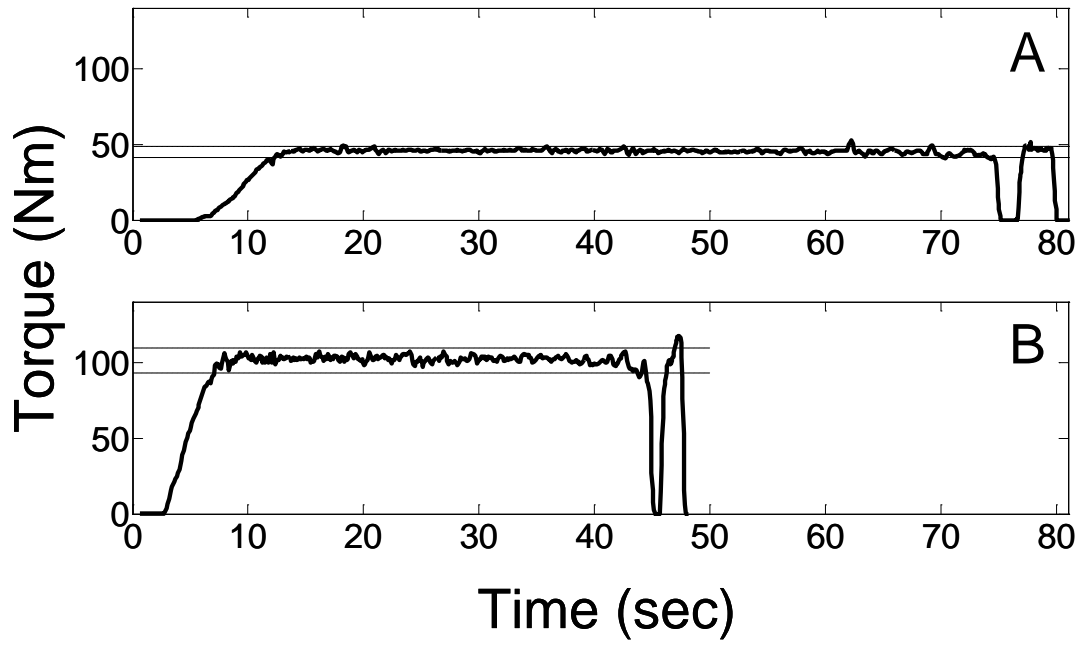
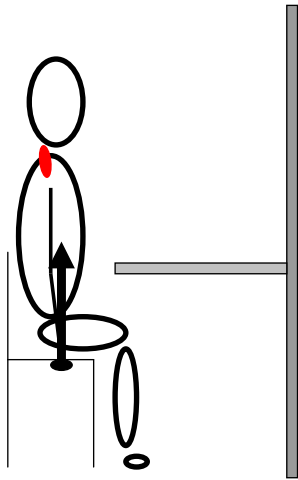


Figure E5



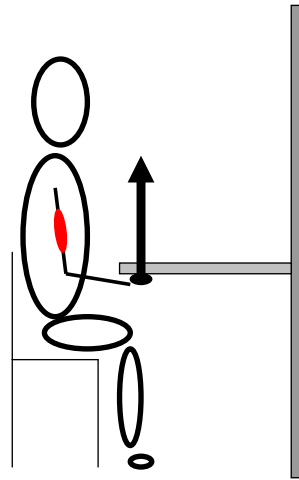
Figure E6

m. Trapezius



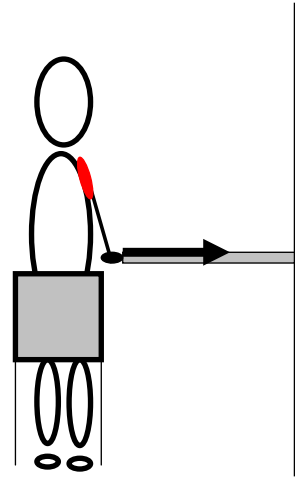
Side view
Position 1

m. Biceps Brachii



Side view
Position 2

m. Deltoideus



Back view
Position 3

Figure E7:

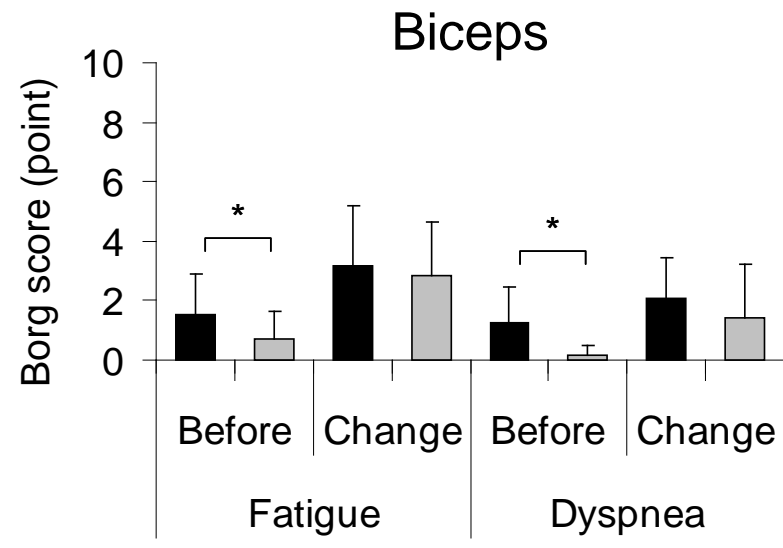
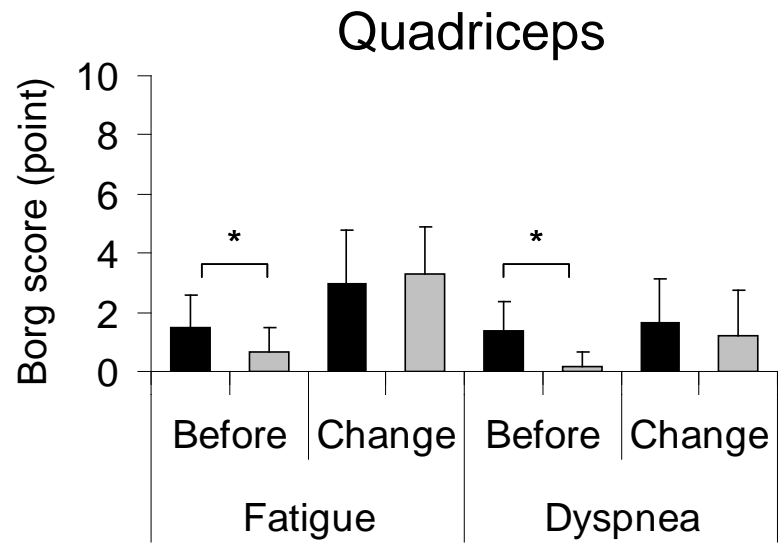


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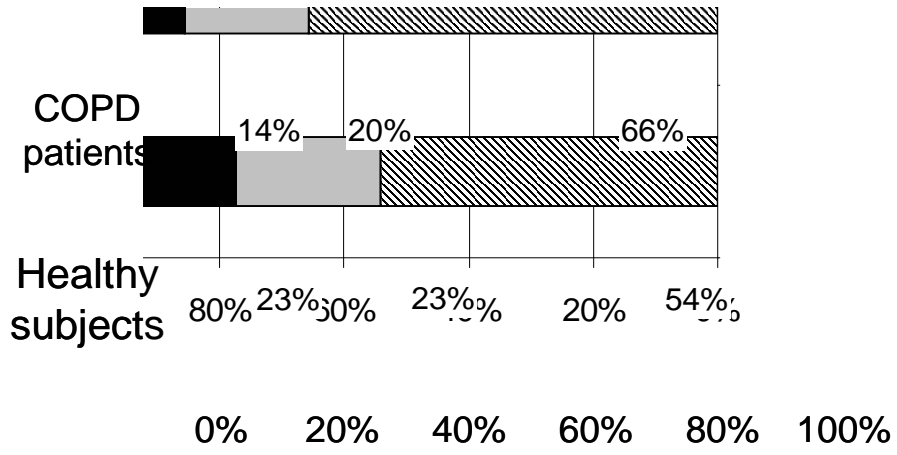


Figure E9

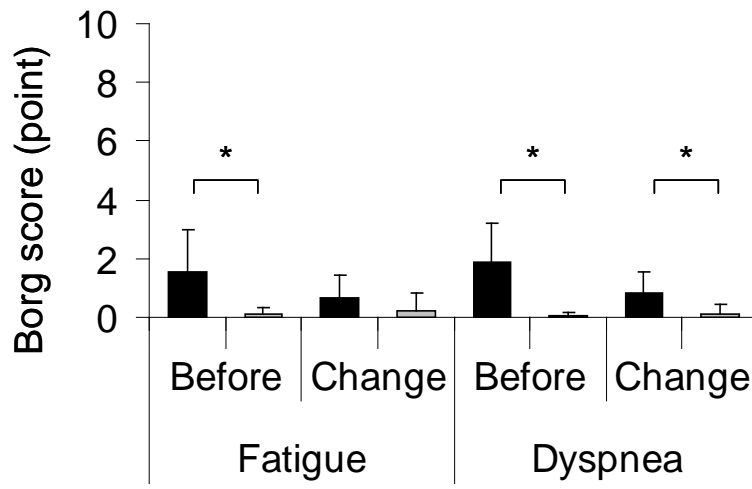


Figure E10:

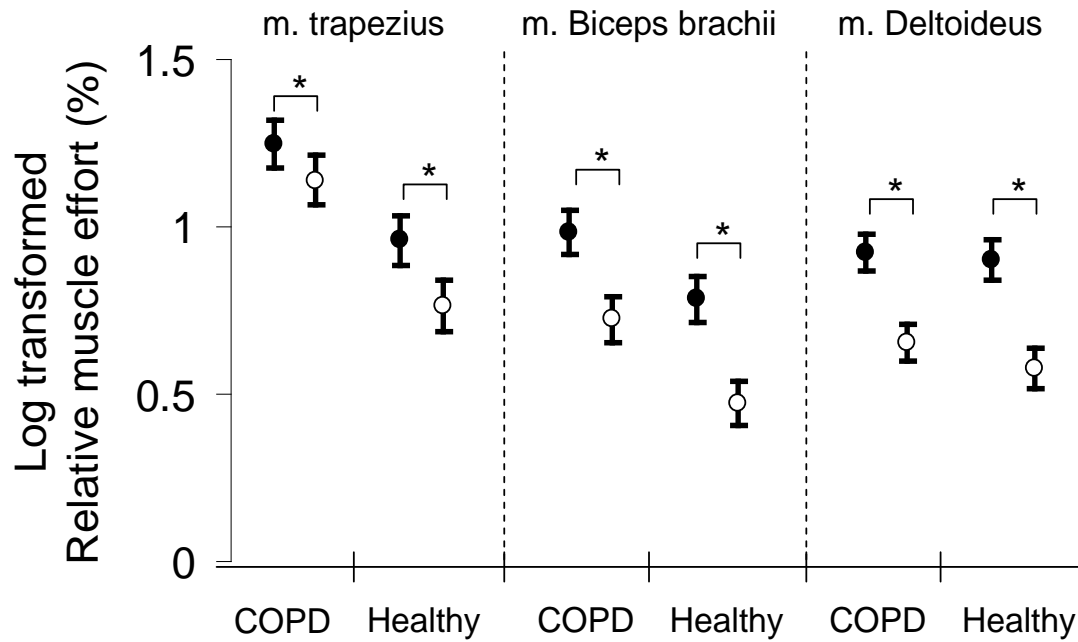


Table E1: Arm intensity (a.u.), arm elevation (a.u.) and leg intensity (a.u) during different arm categories for COPD patients and healthy subjects.

		Arm Intensity (a.u)				Arm Elevation (a.u)				Leg Intensity (a.u)				
		mean	difference	95%CI		mean	difference	95%CI		mean	difference	95%CI		
High	High	COPD	70.0	-12.5*	-15.7	-9.4	-8.0	1.2*	0.5	1.9	7.8	-4.1*	-6.6	-1.6
	High	Healthy	82.6				-9.2				11.9			

	Medium	COPD	76.8	-6.5*	-9.3	-3.6	8.2	-0.5	-1.1	0.1	8.6	-0.5	-2.7	1.7
		Healthy	83.2				8.7				9.1			
	Low	COPD	68.3	-7.7*	-10.7	-4.7	17.5	-0.3	-0.9	0.3	16.2	-3.4*	-5.7	-1.1
		Healthy	75.9				17.8				19.6			
Medium	High	COPD	37.0	0.5	-2.9	3.9	-10.8	0.0	-0.8	0.7	4.3	0.2	-2.5	2.9
		Healthy	36.5				-10.7				4.0			
	Medium	COPD	35.0	-0.8	-3.7	2.2	10.1	1.1*	0.5	1.7	4.6	0.5	-1.8	2.7
		Healthy	35.8				9.0				4.1			
	Low	COPD	33.1	-1.6	-4.3	1.2	18.3	-0.2	-0.8	0.3	19.6	-9.2*	-11.3	-7.2
		Healthy	34.7				18.5				28.8			
Low	High	COPD	8.3	-1.3	-4.4	1.9	-10.5	1.5*	0.9	2.2	1.6	-0.3	-2.8	2.1
		Healthy	9.5				-12.0				2.0			
	Medium	COPD	8.2	-1.2	-4.2	1.9	11.5	1.2*	0.6	1.8	2.3	0.0	-2.4	2.4
		Healthy	9.3				10.3				2.3			
	Low	COPD	8.8	0.7	-2.2	3.6	17.6	-0.1	-0.7	0.5	8.2	3.7*	1.5	5.9
		Healthy	8.2				17.7				4.5			

*: sig. difference between COPD and healthy ($p < 0.05$). Note: arm elevation is calculated using the mean low pass signal in the longitudinal direction (MI). Lower MI means higher arm elevation.

Table E2: geometric means of relative muscle effort (%) during different levels of elevation and intensity of the arm for COPD patients and healthy subjects.

	Trapezius	Biceps	Deltoid

			effort (%)	Ratio of Geometric mean	95%CI	effort (%)	Ratio of Geometric mean	95%CI	effort (%)	Ratio of Geometric mean	95%CI
high	high	COPD	56.7	1.50	0.99-2.27	24.1	1.05	0.70-1.56	35.4	0.90	0.61-1.32
		Healthy	37.8			23.0			39.3		
	med	COPD	38.5	1.94	1.28-2.92	20.4	1.54	1.04-2.28	16.2	1.04	0.72-1.52
		Healthy	19.9			13.3			15.5		
	low	COPD	20.7	1.87	1.23-2.82	12.2	1.17	0.79-1.74	14.4	1.11	0.76-1.62
		Healthy	11.1			10.5			13.1		
med	high	COPD	56.3	1.66	1.09-2.53	23.0	1.21	0.81-1.81	33.6	1.00	0.68-1.47
		Healthy	33.8			19.0			33.6		
	med	COPD	31.7	1.57	1.04-2.37	15.3	1.41	0.95-2.09	11.4	0.92	0.63-1.34
		Healthy	20.2			10.8			12.5		
	low	COPD	15.6	2.15	1.42-3.42	7.9	1.77	1.20-2.63	6.6	1.16	0.79-1.68
		Healthy	7.3			4.4			5.8		
low	high	COPD	44.2	1.71	1.13-2.59	15.5	1.15	0.77-1.71	24.3	1.05	0.72-1.52
		Healthy	25.8			13.5			23.1		
	med	COPD	19.6	1.53	1.01-2.32	6.9	1.12	0.75-1.66	5.7	0.75	0.52-1.10
		Healthy	12.8			6.2			7.5		
	low	COPD	9.9	1.85	1.22-2.78	4.1	1.60	1.08-2.37	3.5	1.18	0.81-1.73
		Healthy	5.4			2.6			3.0		

*: sig. difference between COPD and healthy ($p < 0.05$). Note: A random intercept model analysis was conducted to test significance of the effects. Three-way interactions were present for all muscles. Results of these analyses are described in the main paper. For interpretational purposes: An average relative muscle effort difference on the \log_{10} scale of 0.332 between COPD and Healthy groups (e.g. for trapezius low

elevation/medium intensity) means that on the original scale the relative muscle effort of COPD patients is increased in ca. twofold compared to the healthy group (specifically multiplied by $10^{0.332} = 2.15$).

Table E3: Time spent in different arm categories during arm ADL protocol

Arm category		Time (sec)			
Intensity	Elevation	COPD	Healthy	95% CI	<i>P</i> value
High	High	18 (8)	24 (6)	-11—-1	0.030
High	Medium	31 (15)	42 (12)	-20—0	0.042
High	Low	21 (10)	36 (13)	-23—-7	0.001
Medium	High	18 (8)	15 (9)	-2—9	0.221
Medium	Medium	33 (14)	28 (13)	-5—14	0.334
Medium	Low	50 (20)	44 (16)	-6—19	0.317
Low	High	24 (4)	19 (9)	-1—8	0.110
Low	Medium	27 (9)	23 (13)	-4—12	0.282
Low	Low	39 (14)	30 (11)	-1—17	0.091

Value expressed as mean ± standard deviation (SD)

Abbreviations; CI: Confidence Interval of the mean difference.

